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### **published in**

Journal of Clinical Epidemiology  
2018

### **DOI (link to publisher)**

[10.1016/j.jclinepi.2018.02.010](https://doi.org/10.1016/j.jclinepi.2018.02.010)

### **document version**

Version created as part of publication process; publisher's layout; not normally made publicly available

### [Link to publication in VU Research Portal](#)

### **citation for published version (APA)**

Swaen, G. M. H., Langendam, M., Weyler, J., Burger, H., Siesling, S., Atsma, W. J., & Bouter, L. (2018). Responsible Epidemiologic Research Practice: A guideline developed by a working group of the Netherlands Epidemiological Society. *Journal of Clinical Epidemiology*, 100, 111-119.  
<https://doi.org/10.1016/j.jclinepi.2018.02.010>

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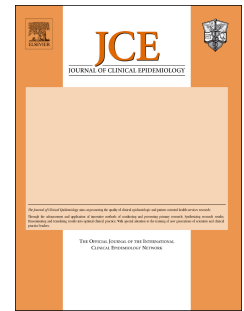
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# Accepted Manuscript

Responsible Epidemiologic Research Practice: A guideline developed by a working group of the Netherlands Epidemiological Society

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PII: S0895-4356(17)30465-1

DOI: [10.1016/j.jclinepi.2018.02.010](https://doi.org/10.1016/j.jclinepi.2018.02.010)

Reference: JCE 9599

To appear in: *Journal of Clinical Epidemiology*

Received Date: 30 April 2017

Revised Date: 22 December 2017

Accepted Date: 1 February 2018

Please cite this article as: Swaen GMH, Langendam M, Weyler J, Burger H, Siesling S, Atsma WJ, Bouter L, Responsible Epidemiologic Research Practice: A guideline developed by a working group of the Netherlands Epidemiological Society, *Journal of Clinical Epidemiology* (2018), doi: 10.1016/j.jclinepi.2018.02.010.

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# Responsible Epidemiologic Research Practice

## A guideline developed by a working group of the Netherlands Epidemiological Society

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## Abstract

**Objectives:** to develop a guideline on responsible epidemiologic research practice that will increase value and transparency, will increase the accountability of the epidemiologists and will reduce research waste.

**Setting:** A working group of the Netherlands Epidemiological Society was given the task of developing a guideline that would meet these objectives. Several publications about the need to prevent Detrimental Research Practices triggered this work. Among these were a series in the Lancet on research waste and a subsequent series on transparency in the Journal of Clinical Epidemiology. The reputation and trust in epidemiologic research is still high and the Netherlands Epidemiological Society wishes to keep it that way. The guideline deals with how epidemiologic research, should be conducted archived and disclosed. It does not deal with the more technical aspects, such as required sample size, choice of study design, etc. The guideline describes each step in the process of conducting an epidemiologic study, from the first idea to the ultimate publication and beyond.

**Methods:** The working group reviewed the literature on responsible research conduct, including the various existing codes of conduct. It applied the general principles from these codes to the elements of an epidemiologic study and formulated specific recommendations for each of these. Next step was to draft the guideline. Preceding the 2016 annual national epidemiology conference in Wageningen a preconference was organized to discuss the draft guideline and to assess support. Support was clearly present and the provided recommendations were incorporated into the draft guideline. In March 2017 a draft version of the guideline was sent to all 1100 members of the society with the request to review and provide comments. All received responses were positive and some minor additions were made. The RERP guideline has now been approved by the board of the Netherlands Epidemiological Society.

**Conclusion:** With the RERP guideline we hope to contribute to better research practices in epidemiology, but perhaps also in adjacent disciplines.

**What is new?** We present a guideline on how epidemiologic research can be conducted in a responsible manner. The guideline will increase transparency and accountability and will reduce research waste.

**Key Words:** Research practice, Research integrity, detrimental research practices, accountability and transparency.

## Introduction

There is ample evidence that scientific research practices are not sound and that study results are not as reproducible as they should be.<sup>1,2,3</sup> Evidence indicates that detrimental research practices in fact are quite common.<sup>4-8</sup> Detrimental research practices are often of a methodological nature and may for instance concern selective reporting of research findings, not reporting the results of a scientific study, protocol deviations not clearly described in the publication, data dredging, and presenting a study as being of hypothesis testing nature although it was set up as an explorative endeavor. A number of cases of research fraud and misconduct served as a wake-up call for the scientific community.<sup>5,9,10</sup> In a meta-analysis of 21 surveys Fanelli reported that 33% of the scientists admitted to having been involved in detrimental research practices and 2% to having been involved in research misconduct at least once in the last 3 years.<sup>5</sup> Research integrity is a topic that is receiving more and more attention.<sup>11,12</sup> Concerns about research misconduct such as fabrication and falsification of data and detrimental research practices have triggered the establishment of several codes of research conduct including for example, the Netherlands Code of Conduct for Scientific Practice<sup>13</sup> the European Code of Conduct for Research Integrity<sup>14</sup> and the Singapore statement on Research Integrity.<sup>15</sup> Furthermore the US National Academy of Sciences has published a report on how it expects scientists to operate.<sup>4</sup>

Concerns about detrimental research practices and research misconduct clearly also apply to biomedical research and by extension to epidemiologic research. A few years ago a series of articles in the January 2014 issue of the *Lancet* voiced concern about how biomedical research is conducted and proposed measures to improve research practice. In the associated commentary, Kleinert and Horton recommended researchers to reconsider how they conduct their studies and how they can contribute to reliable and accessible evidence that addresses the challenges faced by society.<sup>16</sup> In their REWARD (Reducing Waste and Reward Diligence) statement of 2014, also published in *Lancet*, the research waste campaign has set a number of objectives to maximize our research potential (<http://www.thelancet.com/campaigns/efficiency>). In 2009 Glasziou and Chalmers estimated that 85% of today's clinical research may be wasted, not contributing to the advancement of science.<sup>17</sup> In a more recent (2016) series of articles in the *Journal of Clinical Epidemiology* the need for more transparency and accountability in biomedical research was further emphasized.<sup>18,19</sup>

Concern about detrimental research practices in epidemiology is not new. In 1988 the late Alvan Feinstein already described how fraud and deception cause prominent problems in medical research.<sup>20</sup> In 1991 a report on Good Epidemiological Practice was published, providing guidelines on how epidemiologic research in occupational and environmental epidemiology should be conducted.<sup>21</sup> This report already contained elements of responsible epidemiological research practices. Concern about selective reporting, or outcome reporting bias has been substantial in the field of clinical trials, where most evidence on the occurrence of the detrimental research practices has been generated. Currently preregistration of trials for example at the US Government trials register is quite common but still not universally accepted.<sup>8</sup> The All Trials initiative has played a key role in getting preregistration anchored into the legislative framework of the United Kingdom.<sup>22</sup>

Epidemiologic research has had and is likely to continue to have an important role in evidence based public health and clinical medicine. Epidemiologic research findings have greatly

contributed to improving human health by identifying risk factors, evaluating preventive programs, determining the best treatments for disease and care, and providing insight in prognostic factors. Given the limited resources available it is of great importance that biomedical research is carried out according to the best feasible scientific standards. Epidemiology studies cannot be done without the participation of patients or healthy volunteers who invest their time and participate in studies they believe are performed according to the highest feasible standards. Scientists have a responsibility towards these human subjects to collect, analyze and report these data, following responsible research practices. Although much has already been achieved in the form of the codes mentioned above, trials registration and other reporting guidelines (see Equator website: [www.equator-network.org](http://www.equator-network.org)), much work still needs to be done.

Epidemiologists often are perceived and also see themselves as the sentinels of the methods for clinical and public health research. They often participate in multidisciplinary studies because of their valued knowledge and skills with respect to research methodology. Therefore they often are in a good position to promote responsible research practices far beyond their own discipline and have the opportunity to set an example for other research fields as well.

These concerns have led the Netherlands Epidemiological Society to set up the working group Responsible Epidemiologic Research Practice to address this issue. The working group has developed a guideline about how epidemiologic research should be conducted in order to increase value and reduce waste in epidemiologic research and increase transparency and accountability. The guideline does not deal with the contents of epidemiology studies, such as the proper sample size, study design or measuring tools, but it focusses on the process. The guideline applies to all sorts of epidemiology studies and does not provide guidance on specific methodological issues.

The Netherlands Epidemiological Society has a 30-year track record of activities to increase the value of epidemiologic research and training, including the certification of epidemiologists at MSc and PhD level. The reputation of Dutch epidemiologists and of scientists in general is still high and the Netherlands Epidemiological Society is keen on maintaining this. The society therefore encourages its members and other epidemiologists to inform themselves of this document and follow its recommendations. So far the Dutch epidemiologic research community has remained relatively free of fraud cases, but a few of these may ruin this high standing reputation. More importantly, epidemiologic research should meet high quality standards, should be reproducible and should always be relevant to society.

## Methods

In their five year strategic plan for 2016-2020 the Netherlands Epidemiological Society labeled improving the quality of epidemiologic research as one of its key objectives. The RERP working group reviewed recent publications such as the earlier mentioned series in the Lancet on research waste and Responsible Research Practice. The working group held several face to face meetings to review various draft proposals for the guideline. In constructing the guideline it essentially followed the evidence based methodology to develop guidelines, the Evidence Based Guideline Development method.<sup>23</sup> As recommended by this method the working group consulted epidemiologists to obtain their input and to assess their support for the guideline. The working group conducted a systematic review of the literature, but this did not yield any evidence, in support or against, that a guideline to enhance responsible research practice, or components

thereof would be effective. A draft guideline proposal was circulated among the approximately 1100 members of the Netherlands Epidemiological Society and they were invited to provide comments. A preconference to the 2016 annual Dutch conference of the Netherlands Epidemiological Society was organized in which the guideline proposal was discussed and later amended. The final draft was sent to all its members with the request for final commenting in March 2017.

### **Results: The guideline on Responsible Epidemiologic Research Practice**

As stated earlier, several national and international institutions in the scientific community have published codes of conduct for researchers.<sup>13-15</sup> These codes of conduct are aspirational in the sense that they focus on virtues and values, and provide general guidance for the way scientific research should be conducted. Most codes prescribe that scientists should be reliable, impartial, independent, honest, objective and open. These principles need to be translated into concrete behavior and expressed in terms of do's and don'ts. By applying the general principles laid down in these codes of conduct to the entire sequence of an epidemiologic study the working group developed the guideline.

As in many types of other research, in a typical epidemiologic study three phases can be identified. First the study must be prepared. Second, the study is conducted or executed, and third, the study findings are published and the study is archived. This boils down to the following sequence:

1. Preparation of the study
  - a. Setting up the study group
  - b. Constructing a meaningful research question
  - c. Designing a study protocol/grant proposal
  - d. Submitting a grant proposal and obtaining financial support
  - e. Ethical review
2. Conducting the study
  - a. Human volunteers protection
  - b. Data collection
  - c. Statistical analysis
  - d. Preparing report(s)
3. Dissemination and after-care
  - a. Manuscript submission and reporting
  - b. Contact with journalists
  - c. Data archiving and sharing
  - d. Document archiving
  - e. Accountability and transparency

The guideline applies to all of these elements and beyond. The level of detail in documents to be archived should be such that a knowledgeable scientist can reconstruct how the study was conducted and why certain decisions were made. The more details provided the more

transparency is achieved and the better accountable the researchers are. We will now describe in general terms how to do so, following the general sequence of any epidemiologic study.

ACCEPTED MANUSCRIPT



## 1. Study preparation

### 1.a- Setting up the study group

*The first step in any epidemiologic study is establishing the study group.* Scientific research is preferably not conducted in solitude, but by a study group in which scientists work together to collectively design, conduct and report the study. Study groups as a rule are more self-corrective than researchers working by themselves.

The study group should contain sufficient expertise to be able to reliably carry out the entire study throughout all its phases and aspects. Members of the study group should be sufficiently trained to fulfill the tasks they will be responsible for. Each member should be aware what he/she is expected to contribute and what tasks must be performed. It is strongly recommended that at this stage author lists are made for the envisioned publications. In order to avoid disagreement at a later stage it is recommended to also determine the envisioned order of authors, together with their responsibilities. Authors should only be listed if they fulfill the relevant criteria for authorship as for example described by the International Committee of Medical Journal Editors.<sup>24</sup> Conversely, authors who do not perform the tasks as agreed should be removed from the author list. This should be evaluated before manuscript submission. Also, potential conflicts of interest and financial aspects should be discussed within the study group at this stage and the way these will be handled.

### 1.b- Constructing a meaningful and relevant research question

Any sound and reliable scientific study needs to be carefully designed and planned. *The first task of the study group is to define the aim of the study, or the specific hypothesis or research question to be tested.* A thorough systematic review of the existing literature on the study aim should form the basis of the decision whether to conduct a certain study. Chalmers et al recommend that any study proposal should include a systematic review of the literature to justify the need for this new study.<sup>25</sup> Researchers should take into account what is already known about the topic at issue, what their proposed research will add and to what societal expense this new knowledge can be generated. If evidence is sparse such an approach can be too sophisticated, but the study group should convince itself that they have a good understanding of the available evidence.

Researchers should start documenting their work from this phase onward, so they can later disclose how they have derived their definitive research question.

### 1.c- Designing a research grant proposal and the study protocol

*Every epidemiologic study, with the aim of publishing the results should be based on a detailed study protocol. The level of detail should be such that another study group would be able to carry out the study as intended with the protocol in hand.* It is the responsibility of the entire study group to produce the research grant proposal and the study protocol.

A grant proposal can serve as study protocol if it has the necessary level of detail required for a study protocol. Grant proposals are intended to obtain the necessary resources for a study and

may not yet describe the planned study in all its relevant details and finesse. In that case the study group will have to prepare a detailed study protocol prior to starting the study as soon as funding is obtained.

The study group should ensure that adequate research methods are used. These methods should meet the standards of the research field. Research using suboptimal research methods is considered unethical and adds to the body of research waste. Before the study group starts conducting the study a protocol should be written and agreed upon. Ideally the protocol contains a description of the research design, justification of the study population and sample size, a data management plan with quality assurance and auditing steps, and the statistical analysis plan. It should also contain a list of envisioned publications and authors who will contribute to each publication. *It is strongly recommended that the study protocol is made public, either by placing it on a publicly accessible website or by uploading it in an appropriate studies register. Prepublication of the protocol strongly enhances transparency and future accountability.* There might be occasions where the study group decides not to disclose a study protocol prior to publication of the study results, for example the development of a new drug or medical treatment, or innovative discovery. In such cases a copy of the protocol should be deposited in a suitable registry without making it publicly accessible that will treat it as confidential until the study is completed, for example a notary. Then, once the study is completed the deposited copy can be disclosed.

#### **1.d- Submitting a grant proposal and accepting financial support**

The entire study group is responsible and accountable for the contents of the grant proposal and no promises should be made to the funding agency or sponsor that will be difficult to keep, without mentioning this. Members of the study group should not be involved in the review of the grant proposal. In addition, members of the study group should disclose at this stage any other sources of funding received and all conflicts of interest that may collide with the funding sought.

On the other hand, the study group should only accept funding if an independent execution of the entire study, including full disclosure of the results, without any interference of the sponsor is guaranteed. No publication vetoes are acceptable and stopping rules should be formulated carefully. It is acceptable that the sponsor may claim the right to see the results prior to disclosure and have a reasonable embargo period, but it should not be in the position to unreasonably delay or block publication or influence how the results are disclosed.

#### **1.e- Ethical review**

Epidemiologic studies involving human subjects are required to be reviewed by an appropriate ethical review committee. Ethical review must be successfully completed prior to the start of data collection. In most Western countries all intervention studies on human subjects must be reviewed by a certified ethical committee. Observational studies on humans may not necessarily be reviewed by an ethical committee, but we recommend the study group to verify the need for review with the ethical review committee. In the case review is not necessary, a waiver must be obtained.

## **2. Conducting the study**

*The epidemiologic study should be carried out in accordance with the study protocol. Protocol deviations should be recorded and reported with the reasons why these were deemed necessary. Alternatively the protocol can be amended, but these amendments must be clearly identifiable.*

## **2.a- Human volunteers protection**

In case the epidemiology study includes human volunteers the internationally accepted guidelines should be followed (see e.g. declaration of Helsinki <sup>26</sup>). Human volunteers should be well informed about the study and about what is asked from them and should all sign an informed consent form that is archived in the study records. Risks and burdens should be clearly explained and should be acceptable and proportional to the potential benefits of the study. Human volunteers should be treated with respect and their privacy should be well guarded. Human volunteers are protected by law and the pertinent regulations must be adhered to.

## **2.b- Data collection**

The data collection phase should also be carried out in accordance to the protocol. Protocol deviations should be documented, reported and motivated. Quality checks and checks for completeness should be included. Datasets should be checked for accuracy by means of manual checks and by running frequency tables and cross tabulations to identify errors. Copies should be stored in secure places. *The data collection process is a vital element of any study and therefore should be documented in detail.* A digital log, analogous to the lab journal in laboratories should be part of this documentation process.

## **2.c- Statistical analysis**

Prior to the statistical analysis the raw dataset should be finalized. No changes to the raw dataset should be made once the statistical analysis has started. Again, *the statistical analysis should be conducted according to the protocol.* Often additional analyses will be conducted that were not foreseen at the time of protocol development. These should be clearly explained in the report. Journal reviewers may request additional analyses. As these were obviously not foreseen in the study protocol it must be mentioned in the publication.

Protocol adherence should not be so rigorous that the data are not optimally analyzed. Both unplanned and planned but not conducted analyses should be reported and motivated.

The syntax files of all conducted analyses should be stored as key document and archived and preferably made public.

## **2.d- Preparing report(s)**

Preparation of the report is a responsibility of the entire study group. *The report must be an accurate, balanced and concise reflection of the conducted study, taking into account existing reporting guidelines and it should describe its limitations and any deviations from the protocol.* The report can be in the form of one or more scientific publications. Explorative analyses must be identified as such in the publications.

## **3.- Dissemination and archiving**

*A scientific study is only completed when all its results are properly reported and disclosed and when the study has been well documented and archived.* Documentation and archiving should be done in such a way that a trained scientist, not necessarily an epidemiologist, can reconstruct how the study was conducted. Ideally the report(s) must fully document the conducted study, but in most cases it will not contain every detail of the study. Therefore all epidemiologic research with the aim of publishing it should be based on a detailed study protocol. Caution should be taken in publishing results from non-protocolized research in order to avoid publication bias and outcome reporting bias. As an exception non-protocolized research can be published, under the condition that this is clearly stated in the publication. In addition, explorative research, in which multiple analyses are conducted, is regarded as publishable, under the condition that this is clearly stated in the methods section and clearly pointed out in the discussion section and abstract.

### **3.a Manuscript submission and reporting**

Editorial instructions must be followed when submitting a manuscript for publication. Conflicts of interest must always be disclosed in the publication.

There is no objection to writing multiple manuscripts about a study as long as the content is distinctively different and this is not aimed at merely publishing as many reports as possible. If the multitude of results requires writing several publications, they should within reason be cross-referenced so readers are aware of the other publications. The contributions to the manuscript of all authors must be as described in the protocol.

*Any protocolized study must be published.* In the unlikely situation that no scientific journal is willing to accept the manuscript it should be disclosed at the website of the responsible institution or the register where the study was pre-registered or in any other form that is publicly accessible. In case of a study remaining unpublished it is very important to document the trail of manuscript submissions and other circumstantial reasons for not publishing the results.

### **3.b- Contact with media**

Contacts with journalists are an optional part of the dissemination process, after the reviewed manuscript has been accepted for publication and preferably published. *The study and its results should be presented to journalists in a reliable and balanced manner, without making the results appear to be more (or less) spectacular than they really are.* Authors should take efforts to ensure that the text to be published in the journalistic product is accurate, precise, correct and understandable for the readers.

### **3.c- Data archiving and data sharing**

*Once the report is in a final form, the study group must ensure that the raw data files and the final dataset used for the statistical analysis are securely stored, protecting privacy of subjects and be accompanied by a fully explanatory data description or code book.*

*Data sharing is encouraged and should be the norm, since re-use of data makes research more useful and cost-effective.* However, this secondary use should be in accordance with the guideline for Responsible Epidemiologic Research Practice.

Most sponsors do not specify ownership of the data. In that case the study group must consider itself (or more formally the institution) the owner of the data, with all the benefits but also all the responsibilities of good ownership. If a sponsor insists on being the owner, the study group must consider refraining from accepting the grant if external ownership is deemed incompatible with the standards of the study group. Research data should only be shared for re-use if the secondary analyses are compatible with the approval obtained from the ethical review committee. In case of doubt this committee should be asked to review the request for data sharing. In this respect we refer to findable, accessible, interoperable and re-usable (FAIR) guiding principles for scientific data management and stewardship (<https://www.ncbi.nlm.nih.gov/pubmed/26978244>)

### 3.d- Document archiving

A study consists of more documents than the protocol, the dataset, statistical analysis, syntax, results and final report(s). For transparency and accountability reasons it is recommended that other documents, such as questionnaires, meeting minutes, conference presentations, interim reports etc. are also stored for future reference. As example of a storage facility we refer the reader to “Dataverse”, which has been set up by an international community of academic institutions to store datasets, syntaxes etc.<sup>27</sup> This facility is access controlled. Researchers can choose the level of access preferred. Another example is DANS, the Dutch network of data storage for academic institutions.

Which documents should be archived? As a general rule archiving should be such that a well-trained scientist, not necessarily an epidemiologist will be able to reconstruct in detail how the study was conducted and also be able to repeat the study. The archive must also contain all relevant details for an investigation or an audit that may be requested by a scientific journal or a committee investigating an allegation of a breach of research integrity. The box below, containing the key products or “deliverables” produced in the earlier described elements of the epidemiologic study that should be stored in the study archive. Ideally this archive is publicly accessible on a website or in a registry or repository

Study element	Deliverable
1a. the study group	Minutes of the relevant meetings
1b. meaningful research question	A statement describing the study hypothesis and/or study objective
1c. research protocol/grant proposal	Copy of protocol and/or grant application, with sufficient detail to enable a trained scientist to reconstruct the entire study
1d. grant submission	Agreement with funding agency and terms of conditions

1.e ethical review	Copy of the ethical committee approval if required
2a.human volunteers protection	Informed consent and Informed Patient information
2b.data collection	Raw database, code book, data collection log
2c. statistical analysis	Syntax, program files
2d. report preparation	Final report, as intended for submission to contractor and or journal and a copy of the publication(s)
3a.manuscript submission and reporting	Correspondence with editors
3b. contacts with media	Press release or similar documents and the media coverage
3c. data archiving and sharing	Documents and agreements with third parties who obtained access to the data
3d.document archiving	Index of archived documents and files

### 3.e- Accountability and transparency

*Throughout the study execution, but also after the study has been finalized, the study group is accountable for its work.* Requests from third parties to explain and elucidate the study should be taken seriously and – within reason - complied to. The task of being a corresponding author of a publication comes with the responsibility to answer questions from interested parties, within a certain limit of reason. Issues arising from the conduct of the study, in which the study group is held accountable should also be dealt with accordingly. Accountability of study group members is not restricted to their own individual contribution. It encompasses the contributions of the other members as well. In case of concern about research misconduct or detrimental research practices by a member of the study group, or as a whole proper action should be taken, for example by discussing this with the entire study group or even by reporting this to the appropriate Research Integrity Authority.



## Discussion

Responsible conduct of research and scientific integrity are topics that are receiving increasing attention in the lay press as well as in the scientific literature. The Netherlands Epidemiological Society has developed the RERP guideline with the aim to make our membership and other researchers better aware of the key issues. We hope epidemiologists and scientists in other disciplines will embrace our guideline and start using it in their day-to-day work. We realize that implementation of these guidelines will cost some effort, both to convince colleagues of the need as well as to set up the infrastructure and training to adhere to these guidelines. Following the guideline during the conduct of an epidemiologic study will lead to some additional administrative burden on the part of the study group. However, there are also short term benefits from a sound documentation and archiving process. A detailed protocol for example will avoid many discussions about the study methods during its actual conduct. It will assist the authors in writing their journal articles and it will facilitate explaining why certain decisions have been made. Furthermore it will avoid the painful discussions about authorship, roles to be performed during the conduct of the study, since they have been defined and documented at an early stage. It would be helpful if a software program can be developed that assists the study group during the conduct of the study and provides reminders and solutions for all the elements and steps involved. Some research institutes already have software in place intended to aid researchers with their projects. At the preconference several were mentioned: Some institutes like NIVEL (Netherlands Institute for Health Services Research) have developed standard operating procedures to be followed for research following specific designs. They also developed an ISO certified quality management system covering all aspects of conducted research. Several universities or university departments (Groningen and Nijmegen) have software in place where critical documents of studies can be deposited.

The Responsible Epidemiologic Research Practice guideline recommends that every scientist should have mastered in his/her basic training, but it also includes recommendations that are fairly new. For example it is basic philosophy of science that any scientific endeavor must be based on a testable hypothesis that can be verified or falsified. On the other hand, the recommendation that any study should be based on a detailed protocol accessible to others and the recommendation that the results of any protocolled study must be published are fairly new insights.

RERP should not result in a box ticking exercise. It should genuinely assist the study group in documenting and archiving the study and thus will increase transparency and accountability. Furthermore RERP should not be considered the single solution to detrimental research practices. More is needed, especially concerning cultural change in research institutions and among scientists, with less focus on output quantity, impact factors and career development but more on responsible research conduct. Epidemiologists should be more open and honest about their research. They should welcome scrutiny and critical remarks from their peers. We strongly believe that the basis of this cultural change lies in educating epidemiologists and also by

implementing RERP in the curriculum of epidemiology courses. Merely drafting a guideline on responsible conduct of epidemiologic research will probably not have a substantial impact on itself. It must be seen as a part of an already ongoing process towards more awareness about responsible research conduct. The Netherlands Epidemiological Society has put an implementation plan in place aimed at further dissemination and implementation of RERP in the Dutch epidemiology community and beyond. So far members of the RERP working group have made five presentations to epidemiological research groups in the country. We aim at expanding these visits and plan to come back to these groups after one or two years to see what has been implemented. Training in research integrity as a whole, but also in the more practical issues as described in RERP should become an integral part of scientific education, preferably starting at an early stage in the curriculum. Scientists might be reluctant to take time or spend resources for responsible conduct of research,<sup>28</sup> but they should realize that a good documentation process for their work already has short term advantages, and certainly will pay off when writing journal articles. Thoroughly thinking through the entire research project before starting and writing it down in the form of a study protocol will avoid unanticipated issues when conducting it and will provide an opportunity to solve these issues at a stage when it is still possible to do so. In addition, the Responsible Epidemiologic Research Practice guideline will probably have a minor effect, if any, of reducing research misconduct in the form of fabrication, falsification or plagiarism. Scientists willing to fabricate data are likely to be willing to fabricate documents mentioned in the guideline as well. The main aim of the guideline is to reduce detrimental research practices, which are more frequent and as a whole have a larger impact than research misconduct.

The main responsibility of implementing and enforcing the guideline does not lie with the Netherlands Epidemiological Society, but rather with the individual epidemiologist, the department he/she works in and ultimately with the employer. One should realize that detrimental research practices or research misconduct by one individual epidemiologist can adversely impact the reputation of the institution and eventually to the epidemiology community as a whole. This also applies to the funding agency or sponsor. Sponsors are encouraged to more closely follow and audit projects that receive funding. They have an obligation to ensure that the funding is well spent and that the study is conducted according to the funded project proposal. The Netherlands Epidemiological Society welcomes recent requirements of several Dutch funding agencies that require researchers to use data management software to ensure quality and documentation. Other stakeholders might also benefit from the guideline. Journal editors may request a statement that the study was conducted following the guideline, and ultimately the reader would have more confidence in the journal article if the authors state it was conducted according to the guideline. The guideline is a first step but not the final one towards enhancing responsible research practice. It can be expected that future developments will require the Netherlands Epidemiological Society to update this document and further develop its contents. The guideline requires more extensive documentation and archiving than before. Some documents are strongly recommended to be disclosed on the internet prior to data collection, including the study protocol. Researchers should



be aware that due to this improved documentation and disclosure the privacy of study participants can become compromised. Sharing data is a virtue, but researchers must be aware of the importance to protect the privacy of the study participants. Principally data sharing is seen as a responsible practice since it makes better use of the limited resources. However, also data sharing is not without responsibility. The data provider should ensure that the data are used properly and that the data receiver understands the data and uses it in a scientifically responsible way. Co-authorship also comes with the responsibility to ensure proper data use and interpretation.

The results of epidemiologic research should preferably be available to all. Therefore open access publishing is supported. However it should not be at the expense of the peer review process. Certain open access journals can increase their profits by publishing as many manuscripts as possible and take peer review less serious. This will have a negative impact on the quality of the published articles. In the long run we are convinced the guideline will demonstrate its merits by means of creating a more transparent and better documented process. While developing the guideline we received many helpful comments from our members. Two suggestions stand out. First an e-learning module would be illustrative and assist epidemiologists to understand the guideline, and second an IT tool should be developed that assists epidemiologists in their daily work in RERP compliance. In conclusion, we have formulated a set of recommendations to our members, that have been taken from our document and are displayed in the box below:

### Set of recommendations

Study element	Recommendation
1a. the study group	The first step in any epidemiologic study is to establish a study group and the responsibilities and accountabilities of its members.
1b. meaningful research question	The first task of the study group is to define the aim of the study, or specific hypothesis to be tested. Include a systematic review of the literature if applicable
1c. research protocol/grant proposal	Every epidemiologic study, with the aim of publishing the results should be based on a detailed research protocol describing the study. The level of detail is such that another research group is able to carry out the study as intended with the protocol in hand. Once final it is required that the study protocol is ultimately made public, either by placing it on a publicly accessible website or by uploading it in an appropriate studies register
1d. grant submission	Be frank about your project and don't promise more than you can deliver
1e. ethical review	Review by appropriate committee
2a. human volunteers protection	The conduct of the epidemiologic study should be carried out in accordance with the study protocol, and by adhering to the Declaration of Helsinki
2b. data collection	The data collection process is a vital element of any study and therefore should be documented in detail. Include a digital log
2c. statistical analysis	The statistical analysis should be conducted according to the protocol.
2d. report preparation	The report must be an accurate balanced and concise reflection of the conducted study taking into account existing guidelines and it should describe its limitations and deviations from the protocol
3a. manuscript submission	A scientific study is only completed when all its results are properly reported and when the study has been well documented and archived Any protocolled study must be published.

3b. contacts with journalists	the study and its results should be presented to journalists in a reliable and balanced manner, without making the results appear to be more (or less) than they really are.
3c. data archiving and sharing	Once the report is in a final form, the study group must ensure that the raw data files and the final dataset used for the statistical analysis are securely stored, protecting privacy of subjects and accompanied by a fully explanatory data description or code book. Data sharing in principle is encouraged and should be the norm, since re-use of data makes research more cost-effective.
3d. document archiving	Throughout the study execution, but also after the study has been finalized, the study group is accountable for its work.

**Funding:** This project did not receive any grant or funding from the public, commercial or not for profit sectors.

## References

- [1] Bouter LM TJ, Martinson BC, ter Riet G.: Ranking major and minor research misbehaviors: Results from a survey among participants of four Worlds Conferences on Research Integrity. *Research Integrity and Peer Review* 2016, 1:17.
- [2] Ioannidis JP: Why most published research findings are false. *PLoS medicine* 2005, 2:e124.
- [3] Ioannidis JP: Why most discovered true associations are inflated. *Epidemiology* 2008, 19:640-8.
- [4] Sciences NAO: Fostering Integrity in Research. <https://www.nap.edu/catalog/21896/fostering-integrity-in-research>
- [5] Fanelli D: How many scientists fabricate and falsify research? A systematic review and meta-analysis of survey data. *PLoS one* 2009, 4:e5738.
- [6] John LK, Loewenstein G, Prelec D: Measuring the prevalence of questionable research practices with incentives for truth telling. *Psychological science* 2012, 23:524-32.
- [7] Chan AW, Hrobjartsson A, Haahr MT, Gotzsche PC, Altman DG: Empirical evidence for selective reporting of outcomes in randomized trials: comparison of protocols to published articles. *Jama* 2004, 291:2457-65.
- [8] Dwan K, Altman DG, Arnaiz JA, Bloom J, Chan AW, Cronin E, Decullier E, Easterbrook PJ, Von Elm E, Gamble C, Gherzi D, Ioannidis JP, Simes J, Williamson PR: Systematic review of the empirical evidence of study publication bias and outcome reporting bias. *PLoS one* 2008, 3:e3081.
- [9] Martinson BC, Anderson MS, de Vries R: Scientists behaving badly. *Nature* 2005, 435:737-8.
- [10] Kornfeldt DS: Perspective: research misconduct: the search for a remedy. *Academic medicine : journal of the Association of American Medical Colleges* 2012, 87:877-82.
- [11] Hiney: [http://www.scienceeurope.org/uploads/PublicDocumentsAndSpeeches/Briefing\\_Paper\\_Research\\_Integrity\\_web.pdf](http://www.scienceeurope.org/uploads/PublicDocumentsAndSpeeches/Briefing_Paper_Research_Integrity_web.pdf). 2015.
- [12] Nath I, Winnacker EL: Responsible research conduct. *Science* 2012, 338:863.

- [13] nwo:  
[http://www.vsnu.nl/files/documenten/Domeinen/Onderzoek/The Netherlands Code%20of Conduct for Academic Practice 2004 \(version2014\).pdf](http://www.vsnu.nl/files/documenten/Domeinen/Onderzoek/The_Netherlands_Code%20of_Conduct_for_Academic_Practice_2004_(version2014).pdf).
- [14] ESF:  
[http://www.esf.org/fileadmin/Public\\_documents/Publications/Code\\_Conduct\\_ResearchIntegrity.pdf](http://www.esf.org/fileadmin/Public_documents/Publications/Code_Conduct_ResearchIntegrity.pdf).
- [15] statement S: <http://www.singaporestatement.org/>.
- [16] Kleinert S, Horton R: How should medical science change? Lancet 2014, 383:197-8.
- [17] Chalmers I, Glasziou P: Avoidable waste in the production and reporting of research evidence. Lancet 2009, 374:86-9.
- [18] Knottnerus JA, Tugwell P: Promoting transparency of research and data needs much more attention. Journal of clinical epidemiology 2016, 70:1-3.
- [19] Kotz D, Tugwell P, Knottnerus JA: How to promote transparency and accountability in clinical and behavioral research. Journal of clinical epidemiology 2016, 70:275.
- [20] Feinstein AR: Fraud, distortion, delusion, and consensus: the problems of human and natural deception in epidemiologic science. The American journal of medicine 1988, 84:475-8.
- [21] Guidelines for Good Epidemiology Practices for Occupational and Environmental Epidemiologic Research. The Chemical Manufacturers Association's Epidemiology Task Group. Journal of occupational medicine : official publication of the Industrial Medical Association 1991, 33:1221-9.
- [22] trials a: <http://www.alltrials.net/>.
- [23] Mettes TG, van Loveren C, van Oirschot BA, van Maanen-Schakel NW, van der Weijden FG, Bruers JJ: [Evidence-based clinical practice guidelines in oral care 2: process and content of evidence-based guideline development]. Nederlands tijdschrift voor tandheelkunde 2015, 122:21-31.
- [24] icmje: <http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html>
- [25] Chalmers I, Bracken MB, Djulbegovic B, Garattini S, Grant J, Gulmezoglu AM, Howells DW, Ioannidis JP, Oliver S: How to increase value and reduce waste when research priorities are set. Lancet 2014, 383:156-65.
- [26] declaration H: <http://www.wma.net/en/30publications/10policies/b3/>.
- [27] Dataverse: <https://dataverse.nl/dvn/>.
- [28] Devereaux ML: Rethinking the Meaning of Ethics in RCR Education. J Microbiol Biol Educ 2014, 15:165-8.

**What is new?**

The Netherlands Epidemiological Society has developed a guideline to enhance responsible epidemiologic research practice.

**What this adds?**

Following the Responsible Epidemiologic Research Practice will reduce detrimental research practices and will increase transparency and accountability

**What is the implication?**

Following the guideline will increase the reliability and transparency of future epidemiologic research

Conflict of interest statement.

I herewith declare that I have no conflicts of interest with the work presented in the manuscript titled: Responsible Epidemiologic Research Practice: A guideline developed by a working group of the Dutch Society for Epidemiology.

In fact this guideline was developed without receiving any grant or support from any organization except the Dutch Society for Epidemiology.

Gerard Swaen